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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,144	10/17/2006	Iichirou Shimomura	64656 (46590)	9423

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,144	SHIMOMURA ET AL.	
	Examiner	Art Unit	
	Jae W. Lee, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-28,31-38,41,42 and 45-51* is/are pending in the application.

4a) Of the above claim(s) *1-15,18-28,33-38,41,42 and 45-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2 filed on 12/12/2006, and 03/01/2006 .

DETAILED ACTION

Application status

The preliminary amendment filed on 12/16/2005 is acknowledged, wherein Applicants have canceled claims 16, 17, 29, 30, 39, 40, 43 and 44.

Claim(s) 1-15, 18-28, 31-38, 41, 42 and 45-51 is/are pending in this application.

Priority

A claim of priority to applications, PCT/JP04/08699, filed on 06/15/2004; JAPAN 2003171188, filed on 06/16/2003; JAPAN 2003391047, filed on 11/20/2003; JAPAN 2004023557, filed on 01/30/2004; and JAPAN 2004030988, filed on 02/06/2004 is acknowledged.

Election

Applicant's election Group V, Claims 31 and 32 in the response filed on 06/28/2007, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim(s) 1-15, 18-28, 33-38, 41, 42 and 45-51 is/are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Objections to the Specification

The abstract of the disclosure is objected to because it does not describe what the SEQ ID NO: 2 or 4 is. It also does not disclose what is new in the art to which the invention pertains.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. See M.P.E.P. 606.01 for further guidance.

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 16, lines 5-11. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The examiner suggests the replacement of Internet citations with appropriate references because Internet pages are subjected to frequent changes and deletions and could be different when the public accesses the Internet page to view the exactly same information.

Appropriate correction for each error is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31 and 32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the

steps. See MPEP § 2172.01. It is noted by the Examiner that the claimed method is drawn to a method comprising "using", and that there are no "real" active steps in the claimed methods. The omitted steps are, i.e., a method comprising binding a prophylactic/therapeutic substance to the protein of claim 1 or a salt thereof, or the partial peptide of claim 3 or a salt thereof, identifying the compound that modulates the activity of the protein of claim 1 or a salt thereof, or the partial peptide of claim 3 or a salt thereof.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31 and 32 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises using a genus of proteins comprising the same or substantially the same amino acid sequence as the amino acid

sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or a salt thereof, or any partial peptide of said protein or any salt thereof.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of [compositions or methods], it must be clear that: (1) the identifying characteristics of the claimed [compositions or methods] have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification discloses only a single representative species of a protein having the amino acid sequence of SEQ ID NO: 2 or 4 that can be used by the claimed method. However, this single disclosed species fails to provide adequate written description for a screening method of using a genus of proteins comprising the same or substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or a salt thereof, or any partial peptide of said protein or any salt thereof.

It is noted by the Examiner that the specification discloses, "[a] partial peptide of SS169 (hereinafter sometimes simply abbreviated as "the partial peptide of the present invention") may be any peptide having the above-described partial amino acid sequence of SS169, and having substantially the same quality of activity to that of SS169" (see

pg. 18, line 4-12). As such, the genus of partial peptides used by the claimed methods are not limited with respect to its structure, provided that it has a similar function.

It is also noted by the Examiner that the specification discloses "substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO: 2 or 4" to be "an amino acid sequence having a homology of about 60% or more, preferably about 70% or more, more preferably about 80% or more, and particularly preferably about 90% or more, to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4" (see pg. 13, lines 33-34 to pg. 14 lines 1-6). As such, the genus of proteins used by the claimed methods are limited to any polypeptide sequence having roughly 60% sequence homology.

However, the specification fails to describe any identification of structural characteristics or properties of (1) any protein having ~ 60% sequence homology to SEQ ID NO: 2 or 4, (2) any partial peptide, and (3) any salt thereof that can be used in the claimed screening method to serve as a useful tool for the development of prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic abnormalities, including what are called lifestyle-related diseases such as obesity, diabetes mellitus, and arteriosclerosis, or as a useful diagnostic marker for these diseases, and a gene encoding the same, according to the specification on pg. 2, lines 25-32. Taken together, the genus of "proteins," "partial peptides" or "salts thereof" used in the claimed methods encompasses widely variant species, having essentially any structure and function. Please refer to the M.P.E.P. section 2163 [R-5] under II, A, 3,

(a), (ii) for more details with respect to sufficient number of representative species that should be disclosed to describe a widely variant genus.

Given the lack of additional representative species of a genus of methods comprising using any protein comprising the same or substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or a salt thereof, or any partial peptide of said protein or any salt thereof, as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for SEQ ID NO: 2 and 4, does not reasonably provide enablement for a screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises using any protein comprising the same or substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or any salt thereof, or any partial peptide of said protein or

any salt thereof as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Claims 31 and 32 are so broad as to encompass a method of using (1) any protein having ~ 60% sequence homology to SEQ ID NO: 2 or 4, (2) any partial peptide, and (3) any salt thereof that may be free of said protein or said partial peptide.

With regard to the use of all "proteins having ~ 60% sequence homology to SEQ ID NO: 2 or 4," "partial peptides" or "salts thereof" in the claimed method, it is noted by the Examiner that not all structurally different proteins, partial peptides and salts thereof would be able to serve as a useful tool for the development of prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic abnormalities, including what are called lifestyle-related diseases such as obesity, diabetes mellitus, and arteriosclerosis, or as a useful diagnostic marker for these diseases, and a gene encoding the same, according to the specification on pg. 2, lines 25-32. For this reason, a screening method for a prophylactic/therapeutic substance for above-mentioned disease would not work if the "proteins having ~ 60% sequence homology to SEQ ID NO: 2 or 4," "partial peptides" or "salts thereof" did not have the desired biological function as with proteins of SEQ ID NO: 2 and 4. Such methods would not enable one of skill in the art to identify substances that ameliorate a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality. Therefore, the disclosure of a screening method using a protein having the amino acid sequence of SEQ ID NO: 2 or 4 does not commensurate with the breadth of claimed methods encompassing the use of all possible "proteins having ~ 60% sequence homology to SEQ ID NO: 2 or 4," "partial peptides" or "salts thereof."

The claims rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the "proteins having ~ 60% sequence homology to SEQ ID NO: 2 or 4," "partial peptides" or "salts thereof" which are used in the claimed methods. Since the amino acid sequence of a peptide determines its structural and functional

properties, predictability of which peptides can be used while obtaining the desired function requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the peptide's structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of different peptides/proteins.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any protein having ~ 60% sequence homology to SEQ ID NO: 2 or 4, any partial peptide or any salt thereof used in the claimed screening methods because the specification does not establish: (A) regions of any protein, partial peptide, and salt structure which may be modified without affecting the desired biological function and/or utility, which can be useful for the development of prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic

abnormalities, including what are called lifestyle-related diseases such as obesity, diabetes mellitus, and arteriosclerosis, or as a useful diagnostic marker for these diseases, and a gene encoding the same, according to the specification on pg. 2, lines 25-32.; (B) the general tolerance of any protein, partial peptide, and salt to modification and extent of such tolerance without affecting the desired biological function and/or utility that are particularly critical in the claimed screening methods; (C) a rational and predictable scheme for modifying any amino acid residue or structure of any protein, partial peptide, and salt with an expectation of obtaining the desired activity/utility; (D) adequate guidance with respect to all possible screening methods comprising using any protein having ~ 60% sequence homology to SEQ ID NO: 2 or 4, any partial peptide or any salt thereof for the purpose of developing prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic abnormalities; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the polypeptide sequence of a protein and its activity/function is not well understood and unpredictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to make and use the claimed methods.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance,

determination of any protein, partial peptide, and salt thereof used in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31 and 32 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lanctot et al. (US Patent Application Publication, US 2003/0125258, published Jul. 3, 2003).

The instant claims are drawn to a screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises using a protein comprising the same or substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or a salt thereof, or the partial peptide of said protein or a salt thereof.

The reference of Lanctot et al. specifically teaches a method of treating osteoblasts with medium containing BP-1 proteins (see Examples 1-4, especially Example 4 on pg. 19). Said reference teaches the cDNA sequence of SEQ ID NO: 2 encoding the amino acid sequence of SEQ ID NO: 9, which is the secreted human BP-1 protein that is identical to the SEQ ID NO: 2 of the instant application (See SCORE, 20070817_151735_us-10-561-144-2.rag). Therefore, teachings of Lanctot et al. anticipate the active step of the claimed methods, which is drawn to the use of a protein comprising the same or substantially the same amino acid sequence as the amino acid sequence starting at Amino Acid No.1 in the amino acid sequence shown by SEQ ID NO:2 or 4 or a salt thereof, or the partial peptide of said protein or a salt thereof.

Conclusion

Claims 31 and 32 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER